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Dopamine Receptors in Brain

Dopamine is an important neurotransmitter in brain, involved in many physiological functions. It is contained within discrete neuronal systems and exerts its actions through specific receptors located in various brain regions. The development of sensitive techniques in recent years to study these receptors and receptor-mediated function in brain has enabled us to examine these parameters in normal and diseased states. Abnormalities of the dopamine neuronal system have been implicated in a number of CNS disorders such as schizophrenia and other psychoses, Parkinson's disease, Huntington's chorea, tardive dyskinesia, attention deficit disorder in children, and the development of certain tumors of the pituitary. Dopaminergic mechanisms have also been postulated to be involved in the mediation of brain reward and thereby implicated in the process of addiction and substance abuse.

Dopamine receptors in brain have been pharmacologically characterized into two subtypes, each existing in high- and low-affinity states discriminated by agonists but not by antagonists. Interconversion between the two affinity states is mediated by magnesium ions and guanine nucleotides. The high affinity states of the D1 and D2 receptors which appear to represent complexes of ligand, receptor and guanine nucleotide binding protein (from purification studies), appear to mediate the functions of the receptor, which have been studied in isolated cell systems such as in pituitary or parathyroid, in which these receptors regulate hormone secretion. The low affinity state of the receptor appears to be one in which the receptor is only loosely associated with the guanine nucleotide binding protein, and to which dopamine has relatively low affinity. The receptors are linked via guanine nucleotide binding proteins to intracellular second messenger systems such as adenylate cyclase and phosphoinositide turnover.

The recent cloning of dopamine receptors has revealed the presence of several variants of the main D1 and D2 sub-classes. The distribution of these variants in brain appears distinctive and holds exciting promise for site-directed therapy, once selective activators and blockers are developed. Most of the variants of the dopamine receptor appear to be products of separate genes, although one example of 2 forms of the D2 receptor arising from alternate splicing of a single mRNA species has been described.

Source: https://www.industrydocuments.ucsf.edu/docs/zfbb0000